

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (withdrawn): A method for directly delivering a substance into an intradermal space within a mammal, the method comprising bolus administration of said substance into the dermis, whereby the administered substance has at least one improved pharmacokinetic parameter relative to the same pharmacokinetic parameter produced upon administration of the same substance subcutaneously.
2. (withdrawn): The method of claim 1 wherein the administering is through at least one small gauge hollow needle.
3. (withdrawn): The method of claim 1 wherein the needle has an outlet with an exposed height between 0 and 1 mm.
4. (withdrawn): The method of claim 1 wherein administering comprises inserting the needle to a depth which delivers the substance at least about 0.3 mm below the surface to no more than about 2 mm below the surface.
5. (withdrawn): The method of claim 4 wherein administering comprises inserting the needle into the skin to a depth of at least about 0.3 mm and no more than about 2 mm.
6. (withdrawn): The method of claim 1 wherein the improved pharmacokinetics is a decrease in T_{\max} .
7. (withdrawn): The method of claim 1 wherein the improved pharmacokinetics is an increase in C_{\max} .
8. (withdrawn): The method of claim 1 wherein the improved pharmacokinetics is a decrease in T_{lag} .

9. (withdrawn): The method of claim 1 wherein the improved pharmacokinetics is an enhanced absorption rate.
10. (withdrawn): The method of claim 1 wherein the substance is administered over a time period of not more than ten minutes.
11. (withdrawn): The method of claim 1 wherein the substance is administered at a rate between 1 nl/min. and 200 ml/min.
12. (withdrawn): The method of claim 1 wherein said substance is a hormone.
13. (withdrawn): The method of claim 12 wherein the hormone is a growth hormone.
14. (withdrawn): The method of claim 13 wherein the growth hormone is human growth hormone.
15. (withdrawn): The method of claim 1 wherein the substance has a molecular weight greater than 1000 daltons.
16. (withdrawn): The method of claim 1 wherein said substance is hydrophobic.
17. (withdrawn): The method of claim 1 wherein said substance is hydrophilic.
18. (withdrawn): The method of claim 1 wherein the needle(s) are inserted substantially perpendicularly to the skin.
19. (withdrawn): A method of administering a pharmaceutical substance comprising administering the substance intradermally through one or more microneedles having a length and outlet suitable for selectively delivering the substance into the dermis over a time period of not more than ten minutes to obtain absorption of the substance in the dermis thereby producing improved systemic pharmacokinetics compared to subcutaneous administration.

20. (withdrawn): The method of claim 19 wherein the improved pharmacokinetics is decreased T_{\max} .
21. (withdrawn): The method of claim 19 wherein the improved pharmacokinetics is an increase in C_{\max} .
22. (withdrawn): The method of claim 19 wherein the improved pharmacokinetics is a decrease in T_{lag} .
23. (withdrawn): The method of claim 19 wherein the improved pharmacokinetics is an enhanced absorption rate.
24. (withdrawn): The method of claim 19 wherein the length of the microneedle is from about 0.3 mm to about 2.0 mm.
25. (withdrawn): The method of claim 19 wherein the microneedle is a 30 to 50 gauge needle.
26. (withdrawn): The method of claim 19 wherein the microneedle has an outlet of from 0 to 1 mm.
27. (withdrawn): The method of claim 19 wherein the microneedle is configured in a delivery device which positions the microneedle substantially perpendicular to skin surface.
28. (withdrawn): The method of claim 19 wherein the microneedle needle is contained in an array of microneedles.
29. (withdrawn): The method of claim 28 wherein the array comprises 3 microneedles.
30. (withdrawn): The method of claim 28 wherein the array comprises 6 microneedles.
31. (previously presented): A method for administering a macromolecular pharmaceutical substance to a patient, the method comprising delivering a bolus of the

substance intradermally via a needle inserted into the patient's skin so that the needle penetrates the intradermal compartment wherein the needle's outlet depth and exposed height of the outlet are located within the intradermal compartment, wherein the outlet has an exposed height of about 0 to 1mm, so that the substance is delivered into the intradermal compartment and distributed systemically exhibiting a higher C_{max} and a shorter T_{max} of the substance, by comparison with subcutaneous administration of the substance at an identical dose and rate of delivery.

32. (previously presented): The method of claim 31 or 67 wherein delivering the substance intradermally comprises injecting the substance intradermally.

33. (previously presented): The method of claim 31 or 67 wherein the administering comprises infusing the substance over a period of from about 2 min to about 10 min.

34. (previously presented): The method of claim 31 or 67 wherein the administering comprises delivering a bolus of the substance over a period of less than 10 minutes.

35. (canceled)

36. (currently amended): The method of claim 73 wherein the needle has a length of from about 0.3 mm ~~0.3 m~~ to about 2.0 mm.

37. (previously presented): The method of claim 73 wherein the needle is a 30 to 50 gauge needle.

38. (previously presented): The method of claim 73 wherein the needle is configured in a delivery device which positions the needle substantially perpendicular to skin surface.

39. (previously presented): The method of claim 73 wherein the needle is in an array of microneedles.

40. (previously presented): The method of claim 39 wherein the array comprises 3 microneedles.

41. (previously presented): The method of claim 39 wherein the array comprises 6 microneedles.
42. (previously presented): The method of claim 31 or 67 wherein the substance is administered at a volume rate of from about 2 microliters per minute to about 200 millileters per minute.
43. (previously presented): The method of claim 42 wherein the substance is administered at a volume rate of from about 2 microliters per minute to about 10 milliliters per minute.
44. (currently amended): The method of claim 42 wherein the substance is administered at a volume rate of from about 10 microliters per minute to about 200 milliliters ~~millileters~~ per minute.
45. (previously presented): The method of claim 31 wherein the substance comprises a polysaccharide.
46. (previously presented): The method of claim 31 wherein the substance comprises heparin molecule or a fragment thereof having anticoagulant activity.
47. (previously presented): The method of claim 31 wherein the substance comprises Fragmin®.
48. (previously presented): The method of claim 31 wherein the substance comprises a protein.
49. (previously presented): The method of claim 31 wherein the protein comprises a human growth hormone.
50. (previously presented): The method of claim 31 wherein the substance comprises Genotropin®.

51. (previously presented): The method of claim 42 wherein the rate is constant, variable or combinations thereof.

52. (previously presented): The method of claim 31 wherein the substance comprises a pegylated protein.

53. (withdrawn): A method for delivering a bioactive substance to a subject comprising: contacting the skin of the subject with a device having a dermal-access means for accurately targeting the dermal space of the subject with an efficacious amount of the bioactive substance and administering a bolus of the substance into the dermis, wherein the pharmacokinetics of the bioactive substance is improved relative to the pharmacokinetics of the substance when administered subcutaneously.

54. (withdrawn): The method of claim 53 wherein the improved pharmacokinetics is a decrease in T_{\max} .

55. (withdrawn): The method of claim 53 wherein the improved pharmacokinetics comprises an increase in C_{\max} of the substance compared to subcutaneous injection.

56. (withdrawn): The method of claim 53 wherein the improved pharmacokinetics is a decrease in T_{lag} .

57. (withdrawn): The method of claim 53 wherein the device has a fluid driving means including a syringe, infusion pump, piezoelectric pump, electromotive pump, electromagnetic pump, or Belleville spring.

58. (withdrawn): The method of claim 53 wherein the dermal access means comprises one or more hollow microcannula having a length of from about 0.3 to about 2.0 mm.

59. (withdrawn): The method of claim 53 wherein said dermal access means comprises one or more hollow microcannula having an outlet with an exposed height between 0 and 1 mm.

60. (withdrawn): A method for delivering a bioactive substance to a subject comprising: contacting the skin of a subject with a device having a dermal-access means for accurately targeting the dermal space of the subject with an efficacious amount of the bioactive substance at a rate of 1nl/min. to 200 ml/min. and delivering the substance into the dermis over a time period of not more than ten minutes; wherein the rapid onset pharmacokinetics of the bioactive substance is substantially improved relative to subcutaneous injection.

61. (withdrawn): The method of claim 60 wherein the pharmacokinetics is a decreased T_{max} .

62. (withdrawn): The method of claim 60 wherein the pharmacokinetics is an increased C_{max} .

63. (withdrawn): The method of claim 60 wherein the pharmacokinetics is a decreased T_{lag} .

64. (withdrawn): The method of claim 60 wherein the pharmacokinetics is an enhanced absorption rate.

65. (withdrawn): The method of claim 60 wherein the dermal access means has one or more hollow microcannula that inserts into the skin of said subject to a depth of from about 0.3 to about 2.0 mm.

66. (withdrawn): The method of claim 60 wherein the dermal access means has one or more hollow microcannula having an outlet with an exposed height between 0 and 1 mm.

67. (currently amended): A method for administering a hydrophobic pharmaceutical substance to a patient, the method comprising delivering a bolus of the substance intradermally via a needle inserted into the patient's skin so that the needle penetrates the intradermal compartment wherein the needle's outlet depth and exposed height of the outlet are located within the intradermal compartment, wherein the outlet has an exposed height of about 0 to 1mm, so that the substance is delivered into the intradermal compartment and distributed systemically exhibiting a higher C_{max} and a shorter T_{max} of the substance, by

comparison with subcutaneous administration of the substance at an identical dose and rate of delivery.

68. (previously presented): The method of claim 31, wherein the macromolecular pharmaceutical substance has a molecular weight of at least 1000 Da.

69. (previously presented): The method of claim 31, wherein the macromolecular pharmaceutical substance has a molecular weight of at least 2000 Da.

70. (previously presented): The method of claim 31, wherein the macromolecular pharmaceutical substance has a molecular weight of at least 4000 Da.

71. (previously presented): The method of claim 31, wherein the macromolecular pharmaceutical substance has a molecular weight of at least 10,000 Da.

72. (previously presented): The method of claim 31, wherein the macromolecular pharmaceutical substance has a molecular weight of greater than 10,000 Da.

73. (previously presented): The method of claim 31 or 67, wherein administering the substance comprises the step of inserting the needle into the subject's skin so that the needle penetrates the intradermal compartment, and the needle's outlet depth and exposed height of the outlet are located within the intradermal compartment.